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Attorney Docket No. 36459-501

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:	Sackstein		
SERIAL NUMBER:	10/042,421	EXAMINER:	Phillip Gambel
FILING DATE:	October 18, 2001	ART UNIT:	1644
TITLE:	HEMATOPOIETIC CELL E-SELECTIN/ L-SELECTIN LIGAND POLYPEPTIDES AND METHODS OF USE THEREOF		

Assistant Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF PRIOR INVENTION UNDER 37 C.F.R. § 1.132

I Robert Sackstein declare and state:

1. I am an associate professor at Harvard Medical School. I received my M.D. and Ph.D. (in immunology) degrees from Harvard Medical School in 1985. I am the named inventor on this application. I have been working in the field of immunology for 30 years.

2. I have reviewed the Office Action dated September 7, 2006. I understand that claims 1-5, 7 and 62-65 are rejected under 35 U.S.C. §102(b) as anticipated by Stamenkovic et al., EMBO Journal 10; 343-348, 1991; "Stamenkovic" as evidenced by Sackstein J. Invest. Dermatol. 122: 1061-1069, 2004 ("Sackstein 2')

3. I make this declaration to rebut the Examiner's rejection, with which I do not agree.

4. I have reviewed the present application in conjunction with the Stamenkovic reference.

5. Stamenkovic teaches that there is an epithelial form of the CD44 polypeptide that is distinct from the hematopoietic/mesodermal form. Specifically, Stamenkovic describes that the epithelial form contains an additional extracellular peptide domain interposed proximal to the membrane-spanning domain and that this additional peptide sequence impairs binding to the extracellular matrix element hyaluronate. Stamenkovic demonstrates these two forms of CD44

by analysis of CD44 transcripts (i.e. RNA) from various cell types. (See Figure 2 in Stamenkovic) Figure 2 is a photograph of an RNA blot and does not indicate that that any CD44 polypeptides were purified from any primary cell line.

6. Stamenkovic does not teach as the Examiner suggests the isolation and source of native CD44 immunoprecipitated from hematopoietic cells. Importantly, Figure 3 of Stamenkovic demonstrates immunoprecipitation of the "hematopoietic form" of CD44 (CD44H) from CD44H transfected COS cells. The COS cell line is derived from kidney cells of the African Green monkey. CD44H-transfected COS cells cannot produce the claimed glycosylated polypeptide as COS cells are known to lack relevant fucosyltransferases (particularly fucosyltransferase VII), which are essential for producing the sialofucosylated selectin binding determinants of the claimed glycosylated polypeptide. Figure 4 of Stamenkovic demonstrates the immunprecipitation of CD44 from carcinoma cell lines (i.e., the epithelial form) not the hematopoietic form.

7. In contrast, the present invention teaches a highly purified (e.g., isolated) preparation of a glycosylated form of CD44. This glycosylated form is reactive with monoclonal antibody HECA-452. HECA-452 recognizes sialofucosylated glycans. The presence of these sialofucosylated glycans confers L-selectin and E-selectin binding.

8. I have also reviewed Sackstein 2 and rebut the Examiner's assertion that Sackstein 2 provides evidence that the claims are anticipated by Stamenkovic. Specifically, I rebut the Examiners assertion that the pending claims lack novelty because of the following statement I made in Sackstein 2:

> Although initially considered to be a novel selectin ligand by the above biochemical criteria, mass spectrometry subsequently revealed that HCELL is not novel *per se*: it is a glycoform of a well-recognized intergral membrane glycoprotein, CD44, that express the CLA epitope (i.e., is recognized by mAb HECA-452).

9. The concept of novelty under United States Patent Law has been explained to me by counsel.

10. The statement above merely acknowledges that the identity of the backbone was a known polypeptide rather than some previously undiscovered polypeptide backbone. The statement was not intended to mean that the unique glycoprotein with a CD44 polypeptide backbone having a particular sialofucosylated carbohydrate structure that binds E-selectin or L-selectin and is reactive with monoclonal antibody HECA-452 was not novel as defined by United States Patent Law.

11. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and that willful false statements may jeopardize the validity of this application and any patent issuing therefrom.

Robert Sackstein

7/5/07
Date

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